

--According to another feature, the invention relates to dendritic cells that are $\alpha v \beta_3$, $\alpha v \beta_5^+$, CCR5 and CCR7, i.e. are devoid of $\alpha v \beta_3^-$ and CCR5 receptors and carry $\alpha v \beta_5$ and CCR7 receptors.--

Page 7, replace the paragraph at line 22 to line 27 with the following paragraph:

--However, it was shown that the maturation of DC induced by TNF- α caused the induction of IL-12 production and a dramatic inhibition of IL-10 synthesis after activation by CD40. Thus mature DC according to the invention are capable of triggering the differentiation of naive T lymphocytes into type 1 T lymphocytes. Furthermore, the addition of PGE2 inhibited IL-10 production, but also IL-12 production by mature DC obtained.--

Page 12, replace the paragraph at line 23 to line 26 with the following paragraph:

-- The results obtained are reported in Figure 2. These results show that, after 6 h of culture with 4 µg/ml of CHX, 60% of the XG-1 myeloma cells exhibited characteristics of early apoptotic cell death, i.e. binding of Annexin-V but non-incorporation of PI.--

Page 12, replace the paragraph at line 29 to line 34 with the following paragraph:

-- The phagocytosis of apoptotic cells represents another mode of entry for antigens and plays a major role in the phenomenon of cross priming. Recently, several phagocytic receptors have been identified on DC obtained in the presence of human sera, and it has been shown that a monocyte conditioned medium (MCM), which leads to irreversible DC maturation, downregulates their expression (6).--

Replace the paragraph beginning page 13, line 34 and ending on page 14, line 1 with the following paragraph:

-- The operation was repeated with six different donors and the mean fluorescence

--The immature DC obtained with GM-CSF/IL-4 did not produce p70 IL-12, but did produce very large amounts of IL-10 after triggering by CD40 (Table V). The addition of IFN- γ together with stimulation by CD40 caused a 30-fold decrease in the production of IL-10 by immature DC activated by CD40. Induction of the maturation of DC with TNF- α caused a dramatic decrease in the production of IL-10 induced by CD40 (10-fold mean reduction), in association with induction of the expression of IL-12. The addition of IFN- γ again inhibited the production of IL-10 by mature DC. This is consistent with previous reports showing that IFN- γ could be a co-factor for the production of IL-12 induced by CD40 (29,30). However, for the test sample from the other three patients, IFN- γ reduced the production of IL-12 by DC obtained in the presence of GM-CSF/IL-4 and TNF- α . Finally, induction of a totally mature DC with TNF- α and PGE2 caused a reduced production of IL-10 and IL-12 after stimulation by CD40, compared with TNF- α alone.--

Replace the paragraph beginning page 15, line 30 and ending on page 16, line 4 with the following paragraph:

--Non-activated T lymphocytes (HLA DR) were purified from healthy volunteers' peripheral blood by two negative selection cycles using microbeads coated with CD14 and CD19 (Dynal, Oslo, Norway), followed by a cocktail of CD16, CD65 and HLA-DR mAbs (Immunotech) and anti-mouse Ig goat microbeads (Dynal). The purity of the CD3⁺ T cells was greater than 97%. Increasing numbers of DC treated with mitomycin (50 μg/ml) were added to 1.5 x 10⁵ allogenic T cells in 200 μl of RPMI, 5% ABS. After 5 days of culture, the

A

DENNISON, SCHEINER, SCHULTZ & WAKEMAN 612 CRYSTAL SQUARE 4 1745 JEFFERSON DAVIS HIGHWAY ARLINGTON, VIRGINIA 22202-3417

T cell proliferation was measured by the incorporation of tritiated thymidine (1 µCi/well) over the last 12 hours. The results were expressed as the mean counts per minute (cpm) \pm standard deviation, determined in sextuplet culture wells.--

Page 24, replace the Table with the following Table:

--Table III

Profile of DC receptors

Culture conditions	Mean % of positive cells (MFI)			
	MR	CD36	ανβ3	ανβ5
XV-HA GM/IL-4	98 (233)	88 (89)	0	87 (43)
XV-HA GM/IL-4/TNF	80 (95)*	37 (47)**	0	68 (32)*
XV-HA GM/IL-4/TNF/PGE2	74 (91)*	25 (33)**	0	58 (36)*

XV-HA = X-VIVO 15 medium, 2% HA

- p < 0.01 by comparison with cells cultivated with GM/IL-4
- p < 0.05 by comparison with cells cultivated with GM/IL-4--

IN THE CLAIMS

Please cancel all claims presently in the application without prejudice or disclaimer of the subject matter thereof, and insert the following new claims:

- --14. (New) A method of obtaining dendritic cells, comprising:
- 1) cultivating for 4 to 6 days, mononuclear cells derived from cytapheresis after mobilization, in a serum-free medium supplemented with human albumin, in the presence of a granulocyte-macrophage colony stimulating factor (GM-CSF) and an interleukin (IL) that blocks differentiation towards the macrophagic pathway;
- 2) adding TNF- α and optionally an inflammatory mediator to the culture medium and